53. (Original) A thermal transfer system as in claim 30 wherein:

the medium is heated or cooled such that the thermal gradient is in a predetermined direction and the heating or cooling occurs at a predetermined rate.

54. (Original) A thermal transfer system as in claim 30 wherein:

the medium is a biopharmaceutical product.

55. (Original) A thermal transfer system as in claim 30 wherein:

the medium includes proteins.

## REMARKS

Reconsideration of the application and allowance of all pending claims are respectfully requested in light of the remarks provided below.

Pursuant to the revised amendment practice under 37 C.F.R. §1.121, a complete listing of all claims in the application is provided showing the status of each claim in parenthetical expression and the appropriate amendment designations in claims 1 and 30, which are the only claims amended by this Amendment and Response to Office Action.

## I. Request for Additional Prior Art

In the Office action, the Examiner asserts that Applicants have not fully disclosed the prior art. Specifically, the Examiner requests further disclosure of the prior art discussed in the "Description of Prior Art" section in the specification of the above-identified application. In response to an Office action issued in SN 08/895,936, Applicants submitted the Second Declaration of Richard Wisniewski in response to this same inquiry. A copy of this declaration is submitted herewith.

Applicants respectfully submit that the first two paragraphs in the "Description of Prior

Art" section in the specification on page 2 of the present invention refer to the 1992 Genentech device disclosed in the 1992 Wisniewski and Wu publication. See Second Declaration of Richard Wisniewski, ¶8, submitted herewith. Applicants also submit that the prior art described in the third paragraph of this section refers to a device having ribs welded to both the core <u>and</u> the interior wall of the vessel. See Second Declaration of Richard Wisniewski, ¶9, submitted herewith. Since the ribs were connected to both the internal core and the interior wall of the vessel, no thermal bridge can be formed by the medium between a fin tip and the interior wall of the vessel. Id. Heat transfer occurs only through the external wall of the vessel. Such vessels can be used in heat storage devices for, e.g., paraffin. Id. Although not relevant to the particular freezing of biopharmaceutical materials, an example of such vessels in which the ribs are connected to the core and the interior wall is found in U.S. Patent Nos. 2,441,376 to Stiening and 2,129,572 to Finnegan.

Applicants respectfully submit and reiterate that all information in their possession and knowledge concerning the 1992 Genentech container disclosed in the 1992 Wisniewski and Wu article has been disclosed to the U.S. Patent Office. Applicants do not posses specific information concerning how close the heat transfer fins extend to the wall of the container, the dimensions of those fins, the diameter of the container and the volume of the container of the 1992 Genentech device. Applicants are not in possession of the 1992 Genentech container or additional material information relating to the container (e.g. diameter, volume of container, dimension of the fins, how close to the wall of the container the heat transfer fins extended) not already disclosed in the 1992 Wisniewski and Wu article. Applicants do not work for Genentech, which, presumably, has exclusive control of the containers and information related to

the containers, if such container or information still exists. Therefore, Applicants have no way in which, and are not required, to obtain actual measured results or computer generated results of the 1992 Genentech container.

Although he does not remember the exact distance between the fin tip and the interior wall of the 1992 Genentech device, Mr. Wisniewski does state in his second declaration, submitted herewith, that there was a large gap between the fin tips and the interior wall of the 1992 Genentech vessel (e.g. greater than 4 inches).

## II. Response to the Election Requirement

### 1. The Office Action Designated Species

The Examiner has also noted that this application contains claims directed to the following patentably distinct species of the claimed invention:

First species: Figures 1 and 2
Second species: Figure 4
Third species: Figure 5
Fourth species: Figure 6
Fifth species: Figure 7
Sixth species: Figure 8
Seventh species: Figure 9, (more than one, maybe)
Eighth species: Figure 10
Ninth species: Figures 11 and 12
Tenth species: Figure 13
Eleventh species: Figure 14; and
Twelfth species: Figure 15 and an in-determinant number of additional species illustrated in Figures 16-19

### 2. Applicant's Election of Invention and Species

Applicants provisionally elect to pursue the species corresponding to the First Species

(Figures 1 and 2), and respectfully submit that claims 1-55 read on the species of Figures 1 and 2. Applicants respectfully submit that all of these claims are generic to the first, third, fourth, fifth, sixth, and seventh species and respectfully submit that upon allowance of the generic claims, Applicants are entitled to consideration of claims to the additional species which are written in dependent form or otherwise include all the limitations of the allowed generic claim.

**3. Applicants' Traversal**

Applicants respectfully submit that the invention is directed to a method and apparatus for processing a biopharmaceutical product. Applicants respectfully submit that (1) all groups of claims are properly presented in the same application; (2) undue diverse searching should not be required; and (3) all claims should be examined together. Applicants respectfully traverse the requirement for restriction and election on the grounds that searching all of the embodiments of the invention would not be unduly burdensome and, in fact, would be necessary to ensure a complete search for a proper examination on the merits of any one of the identified species. It is further submitted that in order to provide a complete and exhaustive search of any of the species as grouped in the Office Action, the search should include the search directed to each of the other species as grouped in the Office Action. Furthermore, since the method claims mirror the apparatus claims, it would not be unduly burdensome to include all of the claims in the same application.

## III. Rejection Under 35 U.S.C. §103(a)

1. Claims 1-5, 7-10, 12-34, 36-37 and 39-55 stand rejected under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over 1992

Wisniewski and Wu publication and the 1986 Kalhori and Ramadhyani article entitled "Studies on heat transfer from a vertical cylinder with or without fins, embedded in a solid phase change medium" ("the 1986 Kalhori and Ramadhyani article").

In the Office action, the Examiner continues to misunderstand the term "thermal transfer bridge" by equating the same to an ice bridge. However, a "thermal bridge" as discussed in the specification requires heat to be transferred therethrough in a particular way, e.g. forming a downward temperature gradient from the heat transfer member to the interior wall (e.g. as depicted in Fig. 3(b) of the present invention). Claims 1 and 30 have been amended to more clearly define the term "thermal transfer bridge." Specifically, claims 1 and 30 now recite that a thermal transfer bridge is formed by the medium and that heat is transferred from the distal end of the structure or heat transfer member through the thermal bridge to the interior wall in response to the interior wall being actively cooled.

The 1992 Wisniewski and Wu article and the 1986 Kalhori and Ramadhyani article, either alone or in combination, fail to disclose or suggest all of the limitations recited in the claims. Specifically, neither the 1992 Wisniewski and Wu article nor the 1986 Kalhori and Ramadhyani article disclose or suggest a distal end of a structure being in close proximity to an interior surface of a container to allow the formation of a thermal transfer bridge that conducts heat into or out of a medium as recited in the claims of the present invention.

In the 1992 Wisniewski and Wu article, the Genentech device includes a freeze-thaw vessel for biopharmaceutical products having an internal heat transfer coil with fins welded to the external surface of the coil pipe, not an elongated pipe centrally positioned. The figure in the article accurately depicts the heat transfer coil and fin arrangement within the vessel. The fins

attached to the coil are very small and thin and were designed only to aid the freezing around the loop pipe in order to increase the relatively small surface area of the pipe (e.g. adding more cold surface area). In the Genentech device, heat is transferred from a location in the gap between the fin and the interior wall to both the fin and the interior wall. The temperature in the gap between the fin and the interior wall increases and then decreases from the distal end of the fin to the interior wall. This temperature distribution occurs because the gap between the distal end of the fin and interior wall is too large. Accordingly, no thermal bridge is formed because heat is not transferred from the fin through the medium in the gap to the interior wall (i.e. downward temperature gradient profile).

The 1986 Kalhori and Ramadhyani article involves the investigation of solidification of a heat storage medium around a smooth vertical cylinder and also a vertical cylinder with fins. However, only the cylinder was cooled during this investigation. The external vessel walls were not actively cooled as required by the claims of the present invention. The cylinder discussed in this article cools and solidifies the medium by building up towards the external walls of the vessel. Therefore, the temperature from the cylinder (or fin attached to cylinder) to the external wall to increases – resulting in an upward temperature gradient profile, not a downward temperature gradient profile as required for a thermal transfer bridge. Moreover, part of the vessel in this article was wrapped with an electrical ban heater to warm the medium from the outside while the cylinder was cooling it. This cooling and heating generates convectional currents in the liquid phase of the medium. Therefore, the process investigated by Kalhori and Ramadhyani in their 1986 article was completely different from the present invention and the Genentech device disclosed in the 1992 Wisniewski and Wu article. Each of these methods

involves different freezing principles resulting in different temperature gradient profiles during freezing, and thus completely different methods and technologies to freeze products.

Therefore, the 1992 Wisniewski and Wu article and the 1986 Kalhori and Ramadhyani article, either alone or in combination, fail to disclose or suggest the method and arrangement of the vessel recited in the claims of the present invention.

Moreover, the 1992 Wisniewski and Wu article and the 1986 Kalhori and Ramadhyani article teach away from the formation of a thermal transfer bridge. Specifically, the 1992 Wisniewski and Wu article teaches that the heat transfer fins "were configured to divide the tank volume into compartments to decrease freezing and thawing time and to reduce cryoconcentration effects." See pg. 136, col. 1. Thus, the 1992 Wisniewski and Wu artile already teaches that the fins aid in forming compartments and there is no need to extend the fins towards the walls. There is simply no suggestion or motivation therefore to extend the fins of the device disclosed by the 1992 Wisniewski and Wu publication towards the interior wall. Also, the 1986 Kalhori and Ramadhyani article teaches heating the outside of the cylinder. Therefore, the temperature will also be higher at the interior wall of the cylinder than the tip of the fin.

Further, neither of these references recognizes the advantages of a thermal bridge and/or the problems or disadvantages of freezing without the formation of a thermal bridge. Because the references do not recognize the advantage of forming a thermal bridge, there is simply no motivation or suggestion to one of ordinary skill in the art to arrive at the claimed invention. In fact, these articles freeze products by completely different ways using completely different methods and principles than the present invention. Moreover, any combination of these references would fail to result in the claimed invention.

Accordingly, Applicants respectfully submit that the claims are patentable over the cited references.

2. Claims 1-5, 7-10, 12-34, 36-37 and 39-56 stand rejected under 35 U.S.C. §103(a) as being unpatentable over the 1992 Wisniewski and Wu publication and/or the 1986 Kalhori and Ramadhyani article and further in view of U.S. Patent No. 3,550,393 to Euwema ("Euwema"), U.S. Patent No. 5,535,598 to Cothern et al ("Cothern"), U.S. Patent No. 2,114,642 to West ("West"), U.S. Patent No. 1,874,578 to Morrison ("Morrison"), and JP 57-58087 to Nakao ("Nakao").

Applicants respectfully submit that Euwema, Cothern, West, Morrison and Nakao, either alone or in combination, fail to cure the deficiencies of the 1992 Wisniewski and Wu publication and the 1986 Kalhori and Ramadhyani article. Specifically, none of these references teach or suggest the formation of a thermal transfer bridge. More specifically, none of these references teach or suggest the formation of a downward temperature gradient from the structure to the interior wall of the container.

Euwema is directed to a liquid cooling tank in which ice builds up initially to seal channels through which the processed liquid flows. There is no freezing of the entire space whatsoever. The disclosed in Euwema includes vanes 36 and 38 that are connected to the interior wall of a pre-cooling tank 8 that surrounds the exterior wall of another precooling tank 10. These vanes extend towards the exterior wall of the pre-cooling tank 10. The liquid that is processed by Euwema is located within cooling tank 4. There are no structures positioned with cooling tank 4. The cooling tank 4, therefore, is not segmented into a plurality of compartments. Moreover, since there are no structures in the cooling tank 4, a thermal transfer bridge does not

form to conduct heat into or out of the liquid in the cooling tank 4.

Cothern is directed to a method and apparatus for freezing large blocks of a juice quickly. Cothern discloses vessel 30 having freezing members 110 extending downwardly into the liquid within the vessel. Refrigerant flow through the freezing members 110 to provide a heat exchange mechanism for removing heat from the liquid within the vessel. Since the freezing members have a lower temperature than the liquid within the vessel, e.g. between the tip of the freezing members and the interior wall, then the vessel disclosed in Cothern does not disclose a thermal transfer bridge because it cannot have a downward temperature gradient from the freezing member to the interior wall of the vessel. In fact, the vessel disclosed in Cothern has the reverse, an upward temperature gradient from the freezing members 110 to the interior wall of the vessel. Therefore, Cothern fails to disclose or suggest the formation of a thermal transfer bridge that conducts heat into and out of the medium.

Morrison is directed to a heat exchange device for use in heating or cooling liquids such as milk, or water or the like. Similar to Cothern, the liquids are cooled in Morrison by a structure within the device. This structure includes hollow blades 7 that communications with a vertical chamber 7 so that heat or cooling liquid circulates therethrough. Since the hollow blades 7 and vertical chamber 7 have a lower temperature than the liquid within the Morrison device, e.g. between the tip of the freezing members and the interior wall, then the device disclosed in Morrison does not disclose a thermal transfer bridge because it cannot have a downward temperature gradient from the freezing member to the interior wall of the vessel. In fact, the Morrison device has the reverse, an upward temperature gradient from the freezing members 110 to the interior wall of the vessel. Therefore, Morrison fails to disclose or suggest the formation

of a thermal transfer bridge that conducts heat into and out of the medium.

The '642 West patent is directed to an apparatus for accelerating the production of frozen articles. The West apparatus includes a cooling unit having an evaporator that provides a plurality of freezing units 4 adapted to receive and contain a refrigerant. The freezing units are stationary and prject down into the freezing chamber 5. The freezing chamber 5 is filled with a predetermined amount of liquid to be frozen. During freezing, the refrigerant will be condensed in a condenser 10 and accumulated in the receiver 11. The compressor 9 is started and evaporation of the refrigerant within the evaporator 3 causes rapid freezing of the contents of the containers because of the direct heat conductivity between the freezing members 4 and the substance to be frozen. Again, similar to Cothern and Morrison, the liquids are cooled in West by a structure within the device. Since the freezing member 4 has a lower temperature than the liquid within the West freezing container 8, e.g. between the tip of the freezing members and the interior wall, then the device disclosed in West does not disclose a thermal transfer bridge because it cannot have a downward temperature gradient from the freezing member to the interior wall of the vessel. In fact, the Morrison device has the reverse, an upward temperature gradient from the freezing member 4 to the interior wall of the container 8. Therefore, West fails to disclose or suggest the formation of a thermal transfer bridge that conducts heat into and out of the medium.

JP 57-58087 to Nakano is directed to a container for a heat accumulating agent. The Nakano container has metallic plates inserted within the container. The heat accumulating agent 3 is fused due to heating, the heat of the fused part of the agent is transferred to the metallic plates 5 to heat the same. The arrows shown pointing to exterior surface of the container around

its entire circumference appear to represent heat being applied to the exterior surface. With heat being applied to the outer surface of the container, there can be no downward temperature gradient from the tip of the metallic plates to the interior wall of the container because the temperature of the container wall is considerable higher than the tips of the metallic plates that transfers heat from the heat accumulating agent 3. Therefore, Nakano fails to disclose or suggest the formation of a heat transfer bridge as required by the claims of the present invention.

Since all of these devices teach different methods and principles of processing materials, there is clearly no motivation or suggestion to combine. Further, even if these references were combined, the combination would still fail to teach or suggest the formation of a thermal transfer bridge as recited in the claims.

Accordingly, Applicants respectfully submit that the claims are patentable over the cited references.

3. Claims 1-5, 7-10, 12-34, 36-37 and 39-56 stand rejected as being unpatentable over any of the prior art and further in view of the conceded prior art discussed on page 1, line 22- page 2, line 17 of the specification.

The prior art discussed on page 1, lines 22-33 discloses the Genentech device which was the subject of the 1992 Wisniewski and Wu article. As Applicants have repeatedly stated, no thermal bridge is formed by the medium in the gap between the distal ends of the fins and the interior wall of the 1992 Genentech device.

Applicants also submit that the prior art described on page 1, line 34 to page 2, line 17 in the specification refers to a device having ribs welded to both the core and the interior wall of the vessel. Since the ribs were connected to both the internal core and the interior wall of the vessel,

no thermal bridge can be formed by the medium between a fin tip and the interior wall of the vessel. Heat transfer occurs only through the external wall of the vessel. Such vessels can be used in heat storage devices for, e.g., paraffin. Although not relevant to the particular freezing of biopharmaceutical materials, an example of such vessels in which the ribs are connected to the core and the interior wall is found in U.S. Patent Nos. 2,441,376 to Stiening and 2,129,572 to Finnegan.

Therefore, the prior art discussed in the specification does not cure the deficiencies of the other prior art cited in the Office Action.

4. Dependent claims 11 and 38 are rejected under 35 U.S.C. §103(a) as being unpatentable over any of the prior art applied to independent claims 1 and 30 above, and further in view of Brown or Gross. Dependent claims 6 and 35 stand rejected under 35 U.S.C. §103(a) as being unpatentable over any of the prior art applied to independent claims 1 and 30 above, and further in view of Nagashio or Koerber. Applicants respectfully submit that these dependent claims are allowable for the same reasons that independent claims 1 and 30 are allowable as set forth above.

Withdrawal of the rejections and reconsideration and allowance of the claims are therefore, respectfully requested.

## IV. Conclusion

For these reasons, it is believed that all of the claims as presently presented are patentable, and that this application is in allowable condition. Accordingly, allowance of the claims is respectfully requested.

Respectfully submitted,

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